



## General

### Guideline Title

Clinical practice guideline for type 2 diabetes.

### Bibliographic Source(s)

Working Group of the Clinical Practice Guideline on Type 2 Diabetes. Clinical practice guideline for type 2 diabetes. Madrid (Spain): Basque Office for Health Technology Assessment, Osteba; 2008 Jul 1. Various p. [291 references]

### Guideline Status

This is the current release of the guideline.

The Basque Office for Health Technology Assessment, Osteba reaffirmed the currency of this guideline in June 2013.

## Regulatory Alert

### FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

#### Drug Withdrawal

- [October 8, 2010 – Meridia \(sibutramine\)](#) : Abbott Laboratories and the U.S. Food and Drug Administration (FDA) notified healthcare professionals and patients about the voluntary withdrawal of Meridia (sibutramine), an obesity drug, from the U.S. market because of clinical trial data indicating an increased risk of heart attack and stroke. Physicians are advised to stop prescribing Meridia to their patients, and patients should stop taking this medication. Patients should talk to their health care provider about alternative weight loss and weight loss maintenance programs.

#### Additional Notices

- [April 8, 2016 – Metformin-containing Drugs](#) : The U.S. Food and Drug Administration (FDA) is requiring labeling changes regarding the recommendations for metformin-containing medicines for diabetes to expand metformin's use in certain patients with reduced kidney function. The current labeling strongly recommends against use of metformin in some patients whose kidneys do not work normally. FDA concluded, from the review of studies published in the medical literature, that metformin can be used safely in patients with mild impairment in kidney function and in some patients with moderate impairment in kidney function.
- [March 22, 2016 – Opioid pain medicines](#) : The U.S. Food and Drug Administration (FDA) is warning about several safety issues with the entire class of opioid pain medicines. These safety risks are potentially harmful interactions with numerous other

medications, problems with the adrenal glands, and decreased sex hormone levels. They are requiring changes to the labels of all opioid drugs to warn about these risks.

## Recommendations

### Major Recommendations

Definitions of the quality of evidence (1-4, I-IV) and the strength of recommendations (A-D, GPP, and CPG) are presented at the end of the "Major Recommendations" field.

#### Diagnostic Criteria and Type 2 Diabetes Mellitus (DM 2) Screening

##### DM 2 Diagnosis

B: The use of glycosylated hemoglobin (HbA1c) is not recommended as a diagnostic test in patients with altered basal glycaemia.

GPP: The performance of studies within the field to assess the diagnostic performance of HbA1c in these situations is recommended.

##### DM 2 Screening

D: An annual diabetes screening is recommended through fasting glycaemia in the population at risk, defined by hypertension, hyperlipidemia, obesity, gestational diabetes or obstetric pathology (macrosomia, repeated miscarriages, malformations), altered basal glycaemia and impaired glucose tolerance at any age; and every three years in patients aged 45 or over, within a cardiovascular preventive structured program.

C: Capillary glycaemia in total blood cannot be recommended as a diagnostic test in the population groups at risk.

#### Prevention of Diabetes in Patients with Intermediate Hyperglycemia

A: Structured programs which foster physical exercise and diet are advised for patients with impaired glucose tolerance or altered basal glycaemia.

A: The use of pharmacological treatments in patients with impaired glucose tolerance or altered basal glycaemia is not recommended.

#### Diet and Exercise

##### Diet

D: The carbohydrate intake should be distributed throughout the day in order to maintain glycemic control, adjusting it to pharmacological treatment.

A: Structured programs which combine physical exercise with dietary guidance, fat intake reduction (<30% of daily energy), between 55% to 60% of carbohydrates of daily energy and between 20 and 30 g of fibre are recommended. Patients with body mass index (BMI)  $\geq 25$  kg/m<sup>2</sup>, must follow a hypocaloric diet.

B: General use of pharmacological treatment for obesity associated with diabetes (orlistat, sibutramine\*, rimonabant) is not recommended. It can be used for specific cases, taking into consideration the associated pathology as well as the possible interactions, contraindications and adverse effects of the different treatments.

\*Note from the National Guideline Clearinghouse (NGC): On October 8, 2010, Abbott Laboratories and the U.S. Food and Drug Administration (FDA) notified healthcare professionals and patients about the voluntary withdrawal of Meridia (sibutramine), an obesity drug, from the U.S. market because of clinical trial data indicating an increased risk of heart attack and stroke. Physicians are advised to stop prescribing Meridia to their patients, and patients should stop taking this medication. Patients should talk to their health care provider about alternative weight loss and weight loss maintenance programs. See the [FDA Web site](#)  for more information.

B: Morbid obesity surgery in diabetic patients with morbid obesity can be recommended in specific cases, taking into consideration the risks and benefits, the patient's preferences, his comorbidity and the technical availability.

B: Omega 3 fatty acid supplements are not recommended in general terms for the diabetic population.

C: The use of omega 3 fatty acids could be used for diabetic patients who suffer from severe hypertriglyceridemia and do not respond to other

measures (diet and drugs).

B: It is not necessary to contraindicate moderate alcohol intake in diabetic patients who have this habit, unless there are medical criteria to do so. In any case, its intake should be limited to a maximum of two to three units per day for men and one to two units per day in the case of women.

D: Fixed menu diets, portion exchange diets or those based on simplified guidelines can be used, depending on the patient, the professionals and the sanitary environment.

#### Exercise

A: DM 2 patients are recommended to perform regular and continuous aerobic and anaerobic intensive physical exercise, or preferably a combination of both. The recommended frequency is three weekly sessions on alternate days, gradual as regards duration and intensity and preferably, under supervision.

#### Glycemic Control

##### Glycemic Control with Oral Anti-diabetic Drugs

##### *HbA1c Target Figures*

D: In general, guidance target figures under 7% for HbA1c are recommendable. However, the target should be based on an individualised assessment of the diabetes complications risk, comorbidity, life expectancy and the patient's preferences. A stricter control is recommended for people with microalbuminuria within the multifactorial intervention context to reduce cardiovascular risk (CVR). Likewise, less strict targets can be appropriate for patients with a limited life expectancy, elderly people or individuals with comorbidity conditions, a prior hypoglycaemia history or patients with long-term diabetes.

##### *Initial Treatment with Monotherapy*

D: If after a three-six months treatment with non-pharmacological measures, no target figures are achieved, it is recommended to begin pharmacological treatment.

D: Hypoglycaemic treatment should be prescribed within a trial period and its reaction should be monitored using HbA1c as a measuring guideline.

A: Metformin is the drug selected for people overweight or suffering from obesity (BMI  $\geq 25.0 \text{ kg/m}^2$ ).

B: Metformin is also the first line option for people not overweight.

C: Metformin is contraindicated for patients with renal failure (serum creatinine over 1.5 mg/dl for men and 1.4 mg/dl for women).

A: Sulfonylureas should be considered as initial treatment when metformin is not tolerated or is contraindicated and it can be used on patients not overweight.

D<sup>GCP</sup>: A daily single dose of sulfonylurea can be useful when there is a suspicion of a problem of therapeutic non-compliance.

B: Glinides can play a role to improve glycemic control in patients with non-routine models (no regular meals or missed meals).

B: Acarbose can be considered an alternative therapy when there is intolerance or contraindication to the rest of oral antidiabetic drugs.

B: Glitazones should not be used as first line drugs.

B: Should the use of a glitazone be considered necessary, it is recommended to use pioglitazone due to its more favourable safety profile.

GPP: Additional trials are required with morbimortality and safety variables to establish the role of the incretin therapy in DM 2.

##### *Associated Therapy After Failure of Initial Monotherapy*

B: When glycemic control is not appropriate in monotherapy, a second drug should be added.

A: Sulfonylureas should be added to metformin when glycemic control is not appropriate.

A: When glycemic control is not satisfactory with a sulfonylurea in monotherapy, metformin should be added.

B: In case of intolerance to sulfonylureas or in patients with non-routine intake models, glinides can be used.

B: Acarbose as alternative treatment for patients who cannot use other oral antidiabetic drugs could be considered.

B: Glitazones are second line drugs within a combined therapy. Their use could be considered individually when there is poor glycemic control as well as intolerance or contraindication to other oral antidiabetic drugs. In this case, the use of pioglitazone is recommended.

B: Glitazones should not be used in diabetic patients with heart failure.

#### *Treatment After the Failure with a Two Drug Associated Therapy*

A: Should there be an inadequate control of glycaemia despite using a double optimized oral therapy, the use of treatment with insulin is recommended.

B: Triple oral therapy can be recommended after an evaluation of the potential cardiovascular risks in specific patients with insulinization problems.

B: Should the use of a glitazone be considered necessary, it is recommended to use pioglitazone due to its more favourable safety profile.

#### *Insulin Therapy*

A: When an insulin treatment is started, it is recommended to maintain the metformin and/or sulfonylureas therapy.

GPP: The need to continue with sulfonylurea or to reduce its dose due to hypoglycaemia risk must be monitored.

A: In patients with DM 2 who require insulinization the generalized use of insulin analogues is not recommended. On the contrary, slow-acting insulin analogues should be used for patients with an increasing risk to night hypoglycaemias. In patients with DM 2, intensive insulinization is required; fast-acting analogues have no advantages.

D<sup>CPG</sup>: When choosing the initial insulin regimen, the preferences of the patient, the risk of adverse effects (especially hypoglycaemia) and costs should be taken into consideration.

#### Screening and Treatment of Macrovascular Complications

D: The located evidence does not permit the provision of a recommendation in favour of ischemic cardiopathy screening among the general asymptomatic diabetic population. More studies are required in selected high-risk population groups.

C: The same measures are not recommended when treating the general diabetic population and the population group which has suffered an acute myocardial infarction (AMI).

C: When the use of a risk table is required to calculate coronary risk in diabetic patients, the tables of the REGICOR project are recommended.

C: Diabetic patients with more than 15 years of evolution, and in particular if they are women, should consider a treatment with acetylsalicylic acid (ASA) and statins, due to its high cardiovascular risk.

B: A treatment with statins is recommended for diabetic patients with coronary risk  $\geq 10\%$  according to the REGICOR table.

D: A treatment with aspirin can be considered for diabetic patients with coronary risk  $\geq 10\%$  according to the REGICOR table.

B: In type 2 diabetic patients with cardiovascular risk  $\geq 10\%$  in the REGICOR table and for whom statins are contraindicated or not tolerated, the administration of fibrates can be considered.

#### *Treatment for High Blood Pressure*

B/D: Patients with high blood pressure and DM 2 without nephropathy should receive treatment to reduce their blood pressure until achieving a diastolic blood pressure (DBP)  $< 80$  mmHg (B) and systolic blood pressure (SBP)  $< 140$  mmHg (D).

A: DM 2 hypertense patients without nephropathy should be treated firstly with an angiotensin-converting enzyme (ACE) inhibitor or a thiazide; or both when it is considered necessary to control blood pressure. An alternative treatment are dihydropyridines calcium antagonists.

B<sup>CPG</sup>: The use of beta-blockers is not recommended unless there is a firm indication for their use, such as ischemic cardiopathy or heart failure.

#### Screening and Treatment of Microvascular Complications

##### *Diabetic Retinopathy Screening*

B: The 45° non-mydiatic retinal camera with a single photograph is recommended as screening method for diabetic retinopathy.

B: For DM 2 patients without retinopathy, a three-year periodicity control is recommended and a two-year periodicity control for patients with mild non-proliferative retinopathy.

### Diabetic Nephropathy

This clinical practice guideline (CPG) only deals with patients suffering from nephropathy at a micro- and macroalbuminuria stage; the treatment of advanced renal failure is not considered.

#### *Diabetic Nephropathy Screening*

C: Microalbuminuria screening is recommended at the initial diagnosis of type 2 diabetic patients and on an annual basis afterwards.

D<sup>CPG</sup>: The morning albumin-to creatinine ratio is the method recommended.

D<sup>CPG</sup>: Should this method not be available, the determination of microalbuminuria during periods of time of 12 or 24 hours, or the use of morning urine dipsticks could be useful.

#### *Treatment for Diabetic Microalbuminuria*

A: Patients with DM and nephropathy (hypertense and normotensive) should be treated with an ACE inhibitor. The angiotensin II receptor antagonist (ARA II) is the alternative treatment when ACE-Inhibitors are not tolerated.

A: The use of the combination ACE-inhibitor – ARA II is not recommended.

D<sup>CPG</sup>: ACE-inhibitors and ARA IIs must be used with caution in patients with suspicion of renal artery stenosis. Plasma creatinine and potassium monitoring is recommended two weeks after the start of the treatment.

A: Patients with DM 2 and nephropathy are recommended a multifactorial intervention (measures on life style and pharmacological therapy) under the supervision of a multidisciplinary team with appropriate training.

### Diabetic Peripheral Neuropathy

A: Tricyclic antidepressants and traditional anticonvulsants are the drugs selected to treat neuropathic pain in diabetic patients. As an alternative (when there is a contraindication of these or they are not tolerated), the use of new anticonvulsants (gabapentin or pregabalin), opioids (such as morphine, oxycodone or tramadol) or duloxetine are recommended.

A: When the response to the treatment is not satisfactory, other drugs with different action mechanisms can be added, monitoring the response and any adverse effects.

B: For milder cases, a topical treatment with capsaicin can be used, assessing its response and the local adverse effects.

### Erectile Dysfunction

A: Phosphodiesterase type 5 (PDE-5) inhibitors are the drugs chosen to treat erectile dysfunction in men with DM 2.

B: In the case of contraindication or intolerance to PDE-5 inhibitors, the following drugs can be used alternatively: intracavernous alprostadil (tolerance and acceptability problems) or apomorphine (doubtful efficacy). The patient's preferences and response to the treatment are to be assessed.

B: In specific patients where it is not possible or desirable to use pharmacological therapy, psychotherapy can be recommended.

GPP: PDE-5 inhibitors are contraindicated for patients who use nitrates for angina.

#### Diabetic Foot. Assessment, Prevention and Treatment

A: In diabetic patients, structured programs for screening, risk stratification, prevention and treatment for the at-risk foot are recommended.

D<sup>GCP</sup>: The professionals who deal with diabetic patients should assess the risk to develop diabetic foot ulcers during the control visits. An annual check-up is recommended in low-risk patients, every three to six months for mild-risk patients, and between one and three months for high-risk patients.

B: Diabetic foot screening must include inspection of the foot and soft tissues, footwear assessment, musculoskeletal exploration, assessment of peripheral arterial disease complemented with the determination of the ankle-arm index in some cases and sensitivity assessment through the monofilament or alternatively, through the tuning fork.

D<sup>GCP</sup>: More in depth monitoring is recommended for elderly patients (>70 years), those with long-term diabetes, residential patients, patients suffering from sight problems, smokers, those with social problems or those who live alone.

B: Education on the appropriate care for diabetic foot within a structured educational program which includes different elements is recommended in order to improve knowledge, foster self-care and reduce the risk of complications.

B: Patients with prior ulcer without severe deformities can use common footwear (well adjusted and well made), while those who suffer foot deformities could benefit from therapeutic footwear.

GPP: Training on how to deal with diabetic foot should be developed among the professionals who deal with these patients.

#### Treatment for Diabetic Foot Ulcers

D: In diabetic foot ulcers, the necrotic tissue should be removed with surgery for better healing. The use of hydrogel dressings as debriding agents can be recommendable for better healing. In the case of severe ischemia, the patient should be referred.

A: Contact splints are the devices chosen to reduce plantar pressure in diabetic patients with non-infected and non-ischemic foot ulcers.

B: Fixed fibreglass splints are an alternative to contact splints, as they require less time and professional staff.

C: Routine culture in diabetic foot ulcers is not recommended as it has a limited diagnosis value.

D<sup>CPG</sup>: Patients with progressive ulcers which do not heal and with clinical symptoms of active infection should receive systemic antibiotic treatment.

D<sup>CPG</sup>: If an antibiotic is used, when choosing it, the potential microorganisms as well as the local resistance patterns should be taken into consideration, as regards broad-spectrum antibiotics which cover aerobes and anaerobes.

D<sup>CPG</sup>: If there is no solid evidence of clinical effectiveness or cost-effectiveness, the health professionals should use dressings which adapt best to their clinical experience, the patient's preferences or the location of the infection, without forgetting the cost.

B: More studies are required to establish the role of colony-stimulating factors in patients with diabetic foot infections.

#### Diabetologic Education

A: People with diabetes should be given a structured education program based on their regularly checked needs during the diagnosis stage and subsequently, on a regular basis.

D: The use of several learning techniques adapted to the patient's personal preferences and integrated within his daily care routine on the long term are recommended.

B: Primary and specialist care teams should foster programs directly aimed to encourage patient participation, adapted to their preferences and aims and which include contents related to their personal experience.

A: Self-monitoring should be recommended to people with DM 2, by fostering the patient's participation.

B: Self-monitoring components may vary, though in general, these should include knowledge of the disease (definition, diagnosis, importance of good control), dietetic and pharmacological treatment, physical exercise, ways to approach any complications, self-care of feet and self-analysis with adaptation of the treatment in selected patients.

A: It is highly recommended that group education on self-care be directed by skilled professionals.

D: Within the medical context the Working Group recommends that these programs are carried out by nurses, both in primary and specialist care.

C: Self-analysis is recommended for the insulinised patient in order to adjust the insulin dose.

D: The frequency of self-analysis in insulinised patients depends on the characteristics of the patient, the aims to be achieved and the type of insulin.

A: Self-analysis is not recommended for non-insulinised DM 2 patients with acceptable metabolic control and for newly diagnosed patients.

B: In specific patients with inadequate glycemic control, self-analysis can be offered within an educational and self-control structured program with a regular follow-up. To this end, the patient's level of motivation, his abilities and preferences are to be taken into consideration, as well as the frequency of hypoglycaemias, the type of medical treatment used and the costs.

D<sup>CPG</sup>: Self-analysis can be offered to non-insulinised DM 2 patients in order to: provide information on hypoglycaemias, assess glycemic control after changes in medical treatment or life style and monitorize the changes during intercurrent diseases.

#### Definitions:

Levels of Evidence from the Scottish Intercollegiate Guidelines Network (SIGN) for Interventional Studies

1++ High-quality meta-analysis, systematic reviews of clinical trials, or clinical trials with a very low risk of bias.

1+ Well-conducted meta-analysis, systematic reviews of clinical trials or well-conducted clinical trials with a low risk of bias.

1- Meta-analysis, systematic reviews or clinical trials with a high risk of bias.\*

2++ High-quality systematic reviews of case-control or cohort studies. High-quality case-control or cohort studies with a very low risk of bias and with a high probability that the relationship is causal.

2+ Well-conducted case-control or cohort studies with a low risk of bias and a moderate probability that the relationship is causal.

2- Case-control or cohort studies with a high risk of bias and a significant risk that the relationship is not causal.\*

3 Non-analytic studies, such as case reports and case series.

4 Expert opinion.

*\* Studies rated as 1- and 2- must not be used in the recommendations preparation process due to their high possibility of bias.*

Levels of Evidence from the Oxford Centre for Evidence-Based Medicine for Diagnostic Studies

Ia Systematic review with homogeneity of level 1 studies

Ib Level 1<sup>a</sup> studies

II Level 2<sup>b</sup> studies; systematic review of level 2 studies

III Level 3<sup>c</sup> studies; systematic review of level 3 studies

IV Consensus; expert opinion without explicit critical appraisal

<sup>a</sup> Level 1 studies follow:

Blinded comparison to a valid reference test ("gold standard")

Appropriate spectrum of patients

<sup>b</sup> Level 2 studies have only one of these biases:

Non-representative population (the sample does not reflect the population group where the test will be implemented)

Comparison with an inappropriate reference standard ("gold standard") (the test to be assessed is part of the gold standard or the outcome of the test to be assessed poses an influence on the carrying out of the gold standard)

Non-blinded comparison

Case control studies

<sup>c</sup> Level 3 studies present two or more criteria in level 2 studies.

Grades of Recommendation from the Scottish Intercollegiate Guidelines Network (SIGN) for Interventional Studies

A At least one meta-analysis, a systematic review or a clinical trial rated as 1++ and directly applicable to the target population of the guideline; or a body of evidence consisting of studies rated as 1+ and demonstrating overall consistency between them.

B A body of evidence composed of studies rated as 2++, directly applicable to the target population of the guideline and demonstrating overall consistency between them; or extrapolated evidence from studies rated as 1++ or 1+.

C A body of evidence composed of studies rated as 2+ directly applicable to the target population of the guideline and demonstrating overall consistency between them; or extrapolated evidence from studies rated as 2++.

D Evidence levels 3 or 4; or extrapolated evidence from studies rated as 2+.

GPP\* Recommended best practice based on clinical experience and the consensus of the development group.

\* On some occasions, the development group presents important practical cases which they consider relevant but that have no scientific evidence. In general, these cases are related to some aspect of the treatment which nobody would normally ask about and which are assessed as "good practice points."

Grades of Recommendation from the Oxford Centre for Evidence-Based Medicine for Diagnostic Studies

Grade of Recommendation	Level of Evidence*
A	Ia or Ib
B	II
C	III
D	IV

\*See the "Rating Scheme for the Strength of the Evidence" field.

The recommendations adapted from other guidelines have been identified with the index CPG (clinical practice guideline).

## Clinical Algorithm(s)

The following algorithms are provided in Spanish in the original guideline document and its appendices:

Diabetes mellitus type 2 (DM 2) diagnostic algorithm and screening

DM 2 treatment algorithm

Beginning of insulinization

Hypoglycemia treatment

- Treatment for a conscious patient (mild/moderate)
- Treatment for an unconscious patient (hypoglycaemic coma)

Assessment of macro- and microangiopathy in the diagnosis and follow-up of DM 2

## Scope

### Disease/Condition(s)

Diabetes mellitus type 2 (DM 2)

### Guideline Category

Counseling

Diagnosis

Evaluation

Management

Risk Assessment

Screening

Treatment

## Clinical Specialty

Cardiology

Endocrinology

Family Practice

Internal Medicine

Nephrology

Nursing

Ophthalmology

Podiatry

Surgery

## Intended Users

Advanced Practice Nurses

Allied Health Personnel

Health Care Providers

Nurses

Patients

Physician Assistants

Physicians

Public Health Departments

Social Workers

## Guideline Objective(s)

To provide the sanitary professionals in charge of diabetic patient care with a tool which will allow them to make better decisions on the problems that the caring of this disease may involve

## Target Population

Patients in Spain seen in an outpatient setting who are at risk for or diagnosed with diabetes mellitus type 2

## Interventions and Practices Considered

## Diagnosis/Screening/Prevention

1. Screening using fasting blood glucose
2. Screening for macrovascular complications
  - Cardiovascular abnormalities
3. Screening for microvascular complications
  - Diabetic retinopathy screening (non-mydratic retinal photograph)
  - Diabetic nephropathy screening (albumin-creatinine ratio; urine dip stick)
  - Diabetic foot screening (foot and soft tissue check-up, footwear assessment, skeletal muscle scan, peripheral artery disease assessment with ankle-arm index and assessment of sensitiveness)
4. Risk assessment (blood pressure, body mass index)
5. Structured programs fostering physical exercise and diet
6. Frequency of diabetes and diabetes-associated complication screening

Note: The following are not recommended:

Glycosylated hemoglobin (HbA1c) in patients with altered basal glycaemia for diagnosis

Capillary glycaemia in whole blood in population at risk for diagnosis

Pharmacologic treatment for impaired glucose tolerance or altered basal glucose

## Management/Treatment

1. Diet modification
  - Fat, carbohydrate, and protein ratios
  - Omega-3 fatty acids for unresponsive severe hypertriglyceridaemia
2. Pharmacologic treatment of obesity only in selected cases (widespread use is not recommended)
3. Bariatric surgery for obesity
4. Frequency of exercise
5. Individualized HbA1c target levels
6. Anti-diabetic monotherapy (metformin, sulfonylureas, glinides, acarbose, glitazones)
7. Combination 2-drug and 3-drug therapy
8. Insulin therapy (generalized use of insulin analogues not recommended)
9. Management of macrovascular complications (statin therapy, aspirin; fibrates in selected cases)
10. Management of high blood pressure (angiotensin-converting enzyme [ACE] inhibitor, thiazides, dihydropyridines calcium antagonists;  $\beta$ -blockers only in selected cases)
11. Management of microvascular complications
  - Nephropathy (ACE inhibitors, angiotensin II receptor antagonists [ARA II]; [combination ACE-ARA II therapy not recommended])
  - Peripheral neuropathy (tricyclic antidepressants, traditional anticonvulsants, gabapentin, pregabalin, opioids [such as morphine, oxycodone or tramadol], duloxetine, topical capsaicin)
  - Erectile dysfunction (phosphodiesterase type 5 [PDE-5] inhibitors, intracavernous alprostadil, apomorphine, psychotherapy)
12. Foot care (frequency of monitoring for ulcers, use of therapeutic footwear)
13. Management of diabetic foot ulcers (hydrogel dressings, contact splints, fixed fiberglass splints, antibiotic treatment, referral in cases of severe ischemia)
14. Ongoing patient monitoring and follow up
15. Structured patient education programs (self-control, self-care, self-analysis)

## Major Outcomes Considered

- Glycemic control
- Morbidity
- Mortality
- Complications associated with diabetes
- Quality of life

# Methodology

## Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

## Description of Methods Used to Collect/Select the Evidence

2008 Original Guideline

Bibliographic review:

- Data bases: Cochrane Library, DARE, Medline PubMed, Evidence Based Review, Embase, CINAHL, Clinical Evidence, IME, IBECS.
- Languages: English, French and Spanish.
- Research structure: in a first phase, preliminary research of Clinical Practice Guidelines and systematic reviews was carried out. As a secondary evidence resource, a Clinical Practice Guideline on glycaemic control and specific Clinical Practice Guidelines on retinopathy, diabetic foot and nephropathy have been included.
- The Clinical Practice Guideline from the El Grupo de Estudio de la Diabetes en Atención Primaria (GEDAPS) group has been used as additional reference material.
- In a second phase, wide research on original studies (randomised clinical trials, observational studies, studies of diagnosis and prognosis tests and clinical prediction rules) was carried out.
- Research period: the research deadline was January 2008. However, a service of bibliographic alert was kept active until May 2008 to include the most relevant updated literature.

2013 Reaffirmation

Medline, Embase, the Cochrane Library, Evidence Updates, UpToDate, Dunamed, Clinical Evidence and the TRIP Database were searched for literature published from 2008 to June 2013.

The developer performed a literature search of primary and secondary sources, clinical practice guidelines (CPGs), clinical trials and systematic reviews. The developer also screened references included in systematic reviews and references of relevant articles were hand-searched for additional studies.

## Number of Source Documents

Not stated

## Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

## Rating Scheme for the Strength of the Evidence

Levels of Evidence from the Scottish Intercollegiate Guidelines Network (SIGN) for Interventional Studies

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Comparison with an inappropriate reference standard ("gold standard") (the test to be assessed is part of the gold standard or the outcome of the test to be assessed poses an influence on the carrying out of the gold standard)

Non-blinded comparison

Case control studies

<sup>c</sup> Level 3 studies present two or more criteria in level 2 studies.

## Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

## Description of the Methods Used to Analyze the Evidence

Assessment of the quality of the studies and evidence summary for each question (see the "Description of the Methods Used to Analyze the Evidence" field) followed the recommendations of the Scottish Intercollegiate Guidelines Network (SIGN).

## Methods Used to Formulate the Recommendations

Expert Consensus

## Description of Methods Used to Formulate the Recommendations

2008 Original Guideline Document

The methodology used is recorded in the "Manual de elaboración de GPC" (Manual on how to Create a Clinical Practice Guideline) from the Ministry of Health and Consumer Affairs.

The steps followed were:

- Setting up the group in charge of creating the guide, which included the following professionals from primary care (medicine, nursing, pharmacy), specialised care (endocrinologists and nursing educators on diabetes) and professionals experienced in the creation of a Clinical Practice Guideline.
- Creating of clinical questions following the Patient/Intervention/Comparison/Outcome format.
- Developing a qualitative study with diabetic patients (focal group and personal interviews) in order to validate and complete the list of questions.
- Formulation of recommendations based on the "formal assessment" or "reviewed judgement" by Scottish Intercollegiate Guidelines Network (SIGN). The evidence classification and rating of the recommendations have been developed with a mixed system which uses the centre's proposal on medicine based on the Oxford evidence for the diagnosis questions and the SIGN evidence for the rest. Controversial recommendations or those lacking evidence have been discussed and decided on by consensus among the production team in a meeting.
- Different scientific associations involved have been contacted: Spanish Federation of Diabetes, Spanish Society of Primary Care Pharmacists (SEFAP), Spanish Society of Family and Community Medicine (SEMFYC), Spanish Society of Primary Care Physicians (SEMERGEN), which are also represented by the production team and expert collaboration.

### 2013 Reaffirmation

In June 2012, an expert committee was convened to review the currency of the guideline using the following process:

- Formulation of key questions considering the previous version
- Searching for new evidence on the questions through a systematic search of the primary and secondary sources
- Evaluation and synthesis of evidence on the basis of explicit criteria
- External review

## Rating Scheme for the Strength of the Recommendations

Grades of Recommendation from the Scottish Intercollegiate Guidelines Network (SIGN) for Interventional Studies

A At least one meta-analysis, a systematic review or a clinical trial rated as 1++ and directly applicable to the target population of the guideline; or a body of evidence consisting of studies rated as 1+ and demonstrating overall consistency between them.

B A body of evidence composed of studies rated as 2++, directly applicable to the target population of the guideline and demonstrating overall consistency between them; or extrapolated evidence from studies rated as 1++ or 1+.

C A body of evidence composed of studies rated as 2+ directly applicable to the target population of the guideline and demonstrating overall consistency between them; or extrapolated evidence from studies rated as 2++.

D Evidence levels 3 or 4; or extrapolated evidence from studies rated as 2+.

GPP\* Recommended best practice based on clinical experience and the consensus of the development group.

\* On some occasions, the development group presents important practical cases which they consider relevant but that have no scientific evidence. In general, these cases are related to some aspect of the treatment which nobody would normally ask about and which are assessed as "good practice points."

Grades of Recommendation from the Oxford Centre for Evidence-Based Medicine for Diagnostic Studies

Grade of Recommendation	Level of Evidence*
A	Ia or Ib
B	II
C	III
D	IV

\*See the "Rating Scheme for the Strength of the Evidence" field.

The recommendations adapted from other guidelines have been identified with the index CPG (clinical practice guideline).

## Cost Analysis

The guideline developer reviewed published cost analyses.

## Method of Guideline Validation

External Peer Review

## Description of Method of Guideline Validation

Selection of a panel of national collaborator experts in the area of diabetes mellitus type 2 (DM 2) was made to elaborate the initial phase of the questions and review the first draft of the Clinical Practice Guideline.

## Evidence Supporting the Recommendations

### Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

## Benefits/Harms of Implementing the Guideline Recommendations

### Potential Benefits

- Appropriate management of type 2 diabetes mellitus (DM 2) and diabetic complications
- Reduced morbidity and mortality from DM 2

### Potential Harms

- Appendix 3 in the original guideline document provides a list of hypoglycaemic drugs, including potential adverse effects, in Spanish.
- Appendix 7 in the original guideline document provides a list of drugs for neuropathic pain, including their potential adverse effects, in Spanish.

## Contraindications

### Contraindications

- Metformin is contraindicated for patients with renal failure (serum creatinine over 1.5 mg/dl for men and 1.4 mg/dl for women).
- Glitazones should not be used in diabetic patients with heart failure.
- Phosphodiesterase type 5 inhibitors (PDE-5) inhibitors are contraindicated for patients who use nitrates for angina.
- Total contact splints are contraindicated in case of osteomyelitis or infection.

## Qualifying Statements

## Qualifying Statements

- Diabetes mellitus type 2 is a disease where medical advances are constantly taking place, both in the diagnosis as well as its handling and treatment. The changes in the diagnostic criteria, marketing of new drugs for glycemic control and the permanent publication of new studies on the efficacy of cardiovascular risk factors must be assessed and incorporated to clinical practice as appropriate by those professionals responsible for the care of diabetic patients.
- This Clinical Practice Guideline focuses on the patient's care within the outpatient context and does not deal with gestational diabetes or the acute metabolic complications of the disease. As regards micro- and macroangiopathic complications, the Clinical Practice Guideline approaches its screening, prevention, diagnosis and partial aspects of the treatment. There are treatments for these complications which are dealt with at primary care and thus justify their approach in this guide. These are the treatments of microalbuminuria, some aspects of neuropathy and diabetic foot.

## Implementation of the Guideline

### Description of Implementation Strategy

An implementation strategy was not provided.

### Implementation Tools

Audit Criteria/Indicators

Chart Documentation/Checklists/Forms

Clinical Algorithm

Foreign Language Translations

Mobile Device Resources

Patient Resources

Quick Reference Guides/Physician Guides

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

## Institute of Medicine (IOM) National Healthcare Quality Report Categories

### IOM Care Need

Living with Illness

Staying Healthy

### IOM Domain

Effectiveness

Patient-centeredness

# Identifying Information and Availability

## Bibliographic Source(s)

Working Group of the Clinical Practice Guideline on Type 2 Diabetes. Clinical practice guideline for type 2 diabetes. Madrid (Spain): Basque Office for Health Technology Assessment, Osteba; 2008 Jul 1. Various p. [291 references]

## Adaptation

Some of the recommendations in this guideline have been adapted from other guidelines, as identified in the "Major Recommendations" field with the indicator "CPG."

## Date Released

2008 Jul 1 (reaffirmed 2013 Jun)

## Guideline Developer(s)

Basque Office for Health Technology Assessment, Osteba - State/Local Government Agency [Non-U.S.]

GuiaSalud - National Government Agency [Non-U.S.]

Ministry of Health (Spain) - National Government Agency [Non-U.S.]

## Source(s) of Funding

Not stated

## Guideline Committee

Working Group of the Clinical Practice Guideline on Type 2 Diabetes

## Composition of Group That Authored the Guideline

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García, endocrinologist, president of the Spanish Diabetes Federation (FED)

## Financial Disclosures/Conflicts of Interest

A declaration of interests has been requested from all the members of the Working Group, as well as from professionals who have participated as expert collaborators (see Appendix 12 of the original guideline document for the Spanish language declarations).

## Guideline Status

This is the current release of the guideline.

The Basque Office for Health Technology Assessment, Osteba reaffirmed the currency of this guideline in June 2013.

## Guideline Availability

Electronic copies: Available in [English](#)  and [Spanish](#)  from the GuiaSalud Web site.

## Availability of Companion Documents

The following is available:

- A quick guide to the clinical practice guideline for type 2 diabetes. Madrid (Spain): Basque Office for Health Technology Assessment, Osteba; 2008. Available in Spanish from the [GuiaSalud Web site](#) . Also available in [Catalan](#) , [Euskera \(Basque\)](#) , and [Galego \(Galician\)](#)  from the GuiaSalud Web site.

The Spanish version of the guideline is also available via a [mobile application](#)  and in [Personal Digital Assistant \(PDA\) format](#)  from the GuiaSalud Web site.

In addition, a variety of tools are available in Spanish in the appendices of the [original guideline document](#) , including coronary risk tables, instructions on the use of monofilament, and proposed assessment indicators.

## Patient Resources

A patient guide for type 2 diabetes is available in Spanish from the [GuiaSalud Web site](#) .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

## NGC Status

This NGC summary was completed by ECRI Institute on July 13, 2012. The information was verified by the guideline developer on July 30, 2012. The currency of the guideline was reaffirmed by the developer in June 2013 and this summary was updated by ECRI Institute on October 29, 2013. This summary was updated by ECRI Institute on April 15, 2016 following the U.S. Food and Drug Administration advisory on Metformin-containing Drugs. This summary was updated by ECRI Institute on June 2, 2016 following the U.S. Food and Drug Administration advisory on Opioid pain medicines.

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